## REMARKS

Applicant wishes to thank the Examiner for the interview held with Applicant's representatives on November 19, 2004. Applicant understands that the Examiner's supervisory examiner, Examiner Chin, was not available to attend the interview and that efforts were subsequently made to convey the contents of that discussion with him. Applicant further understands that a follow up meeting between the Examiner and her supervisor has not occurred to date. So as to assist prosecution of the instant application, Applicant submits this amendment.

With entry of this amendment, claims 1-6 and 8-23 are currently pending. Applicant has amended claims 4 and 5 to correct grammatical errors. Applicant has also introduced new claim 23, which recites a method of detecting and/or quantifying an IgE antibody comprising simulating *in vivo* interactions between the IgE antibody, the IgE antibody's ligand and the IgE antibody's receptor. Support for this claim may be found in the specification at least at page 3, lines 22-30; page 4, line 16 to page 6, line 32; page 9, lines 15-21; page 10, lines 4-8; Example 2; and Example 5.

Applicant acknowledges the Office's withdrawal of the previous rejection of claims 1, 6, 8-16, 21, and 22 under 35 U.S.C. 112, second paragraph. Applicant addresses the remaining rejections below.

### Rejections Under 35 U.S.C. §103

The Office maintains its rejection of claims 1-5, 8-14, 16, 21, and 22 under 35 U.S.C. § 103(a) as allegedly obvious over Johansen (U.S. Pat. 6,087,188) in view of Johnson (U.S. Pat. 6,034,066) and Frank 2 (U.S. Pat. 6,060,326). According to the Office, Johansen teaches a method of detecting an antibody using a ligand bound to biotin; an antibody to the antibody to be detected; a chemiluminescent acridinium

compound bound to avidin; and a method for quantifying specific antibodies. The Office acknowledges that Johansen does not teach using an IgE receptor to detect or quantify IgE. Regarding Johnson, the Office alleges that this reference teaches the role of CD23 in regulating the immune response, such as IgE responses. The Office believes that Frank 2 teaches a method for detecting IgE antibodies using a human Fc epsilon receptor.

The Office argues that it would have been obvious to one of ordinary skill in the art to use the IgE receptors of Johnson and Frank 2 to measure IgE according to the method of Johansen. In addition, with regard to claim 16, the Office believes it would have been obvious to use enough ligand molecules to optimize binding of all the IgE molecules in a sample.

Applicant previously presented three main arguments as to why the pending claims were not obvious in light of these three references. First, the present invention simulates any interference from other immunoglobulins, as well as any other potentially interfering component, present in the sample. For example, for a sample taken from patients who have undergone Specific Allergy Vaccination (SAV) or other immunotherapies, the amount of IgE detected in the sample by the invention would be lower than the total amount of IgE detected by a commercial kit, which uses an anti-IgE antibody instead of an IgE receptor. See Example 2 of the specification. The invention's ability to provide a more accurate assessment of a patient's immune status with regard to IgE activity is due in part to the unique combination of steps recited in the methods of the invention.

The Office now responds by asserting that, because claims 1-6 and 8-22 allegedly do not recite the concept of simulating *in vivo* conditions, Applicant's argument is not relevant. As provided in the Examiner interview of November 19, 2004, Applicant has added new claim 23, which does recite the concept of simulating *in vivo* conditions. Thus, claim 23 is not obvious in light of Johansen, Johnson, and Frank 2. With regard to claims 1-6 and 8-22, Applicants respectfully assert that these claims are not obvious as discussed below.

Second, Applicant noted that the Office did not explain why the skilled artisan would be motivated to pick and choose particular features from the methods of Johansen and Frank 2, at the expense of leaving other features out, and then combining such selected features in order to arrive at the present invention. The Office now responds by referring to column 5, lines 47-56 of Frank 2 for an alleged source of motivation. This portion of Frank 2 provides that "[i]n addition, a $Fc_{\epsilon}R$ formulation of the present invention can include not only a $Fc_{\epsilon}R$ but also one or more additional antigens or antibodies useful in detecting IgE. . . . Examples of antibodies used in the present invention include . . . antibodies that bind selectively to the constant region of an IgE heavy chain . . . or antibodies that bind selectively to an IgE having a specific antigen specificity . . . . " The Office concludes that because Frank 2 allegedly uses the same reagents as the method of Johansen while Johansen teaches the use of these reagents in more explicit method steps. Applicant traverses.

As the Office has acknowledged, Johansen's method used antibodies to detect the presence of IgE, not IgE receptors. In contrast, the Office's citation from Frank 2 discusses a formulation which uses at least an IgE receptor and may or may not use

other reagents like antibodies that bind to different portions of an IgE molecule. Thus, Johansen and Frank 2 do not use the same set of reagents. Moreover, at best, Johnson merely provides a discussion as to the functions of CD23 in the immune system without any reference to using this receptor in a method for detecting or quantifying IgE. Frank 2, uses a different method from the instant invention but uses FcεR.[1] The Office continues to improperly use hindsight in suggesting that it would have been obvious to use CD23 or FcεR in the method of Johansen or that it would have been obvious to optimize detection or quantification by binding all the IgE molecules in a sample.

Applicant's third and final argument pertained to a lack of a reasonable expectation of success. To establish a *prima facie* case of obviousness, the Office must show that the skilled artisan would be motivated to combine these three references as the Office suggests and that the skilled artisan would have a reasonable expectation of success in doing so. As Applicant noted, the methods for detecting IgE disclosed in Frank 2 and Johansen involve different steps and different reagents. The Office has not provided evidence to suggest that there was an expectation that one could successfully extrapolate the use of a reagent (FcεRI receptor) utilized under a particular set of conditions (Frank 2) and expect it to work as a replacement of another reagent (anti-IgE antibody) under a different set of conditions (Johansen). And Johnson, does not even mention the use of an IgE receptor in a method of detecting an IgE antibody.

[1] To clarify the teaching of Frank 2, the Fc receptor discussed in this reference is a canine Fc receptor, not a human Fc receptor as the Office suggests.

Applicant respectfully notes that the Office has not addressed this aspect of Applicant's argument. For the above reasons, Applicant requests that the Office withdraw its rejection of claims 1-5, 8-14, 16, 21, and 22 under 35 U.S.C. § 103(a) as allegedly obvious over Johansen, Johnson, and Frank 2.

Claims 6 and 17-20 remain rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Johansen and in further view of Frank 2 and Arnold (U.S. Patent 6,004,745). According to the Office, it would have been obvious to one of ordinary skilled in the art to add the label molecule after a first separation step and then separating the non-complexed labels as discussed in Arnold using the reagents in the method of Johansen as modified by Frank 2.

As Applicant previously noted, Arnold does not cure the lack of motivation or the lack of a reasonable expectation of success as discussed above. The Office now responds by arguing that it has provided the requisite motivation to combine via its discussion of Johansen and Frank 2 and therefore need not look to Arnold for such motivation. The Office further alleges that Arnold teaches two separation steps, the first to remove antigen that has not bound to immobilized antibodies and the second separation step to remove any labeled, non-immobilized antibodies that have not bound to the antigen.

As Applicant explained above, neither Johansen nor Frank 2 alone or in combination motivate the skilled artisan to derive the instant invention. Arnold does not cure this deficiency. Arnold's method does not use an IgE receptor or mention the use of an IgE receptor. Rather, Arnold uses two antibodies, one immobilized to a surface and the other labeled. With respect to claims 17-19, the Office has not explained why

the skilled artisan would replace *only* the immobilized antibody with an IgE receptor to arrive at the invention instead of replacing both antibodies, which, as alleged by the Office, may provide more specificity and sensitivity to the method. There is no teaching or suggestion anywhere in the cited references that such a single replacement would offer any particular advantage over a double replacement. Moreover, the Office has not explained why one would be motivated to use two separation steps, as allegedly taught by Arnold, in the method of Johansen *and* to further modify this combination by using the formulations described by Frank 2.

In sum, claims 6 and 17-20 are not obvious in view of Johansen, Frank 2, and Arnold. Applicant requests that this rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of pending claims 1-6 and 8-23.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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